

REMARKS

Based on a prior communication from Applicant in response to a restriction requirement, the group of claims 1-4, 8, 9 and 13-15 were pending in the application. Upon entry of the formal election/restriction-based cancellation below, of claims 5-7 and 10-12, and the cancellation of claims 1, 3, 4, and 9 herein, and the addition of new claim 16 (which incorporates limitations of claims 1, 3 and 4), claims 2, 8, and 13-16 remain pending in this case.

It is noted that claim 9 is cancelled as this contains limitations that are now incorporated in claim 8, from which claim 9 previously depended.

The basis for this argument and amendment in this Response/Amendment from Applicant is that the Examiner has indicated, in a telephonic interview on August 4, 2003, that he is willing to consider the following reasoning. Because the Graham et al. WO 98/13510 publication, which was used in a 37 CFR 103(a) obviousness rejection with other references, was not found by the Examiner to sufficiently disclose the limitations of present invention so as to warrant being a document from which priority could be claimed, the same document cannot, on the other hand, contain a suggestion or motivation to combine this publication with other references to render obvious the present invention. Following this reasoning, a 37 CFR 103(a) obviousness rejection using the Graham et al. WO 98/13510 publication is inappropriate because neither this nor the other references contain a suggestion or motivation to combine the recombinase-based technology in WO 98/13510 with the other references to obtain the present invention.

Election/Restriction

To comply with the Examiner's request for a complete reply to the Final Office action, Applicant herein cancels the non-elected claims, claims 5-7 and 10-12. Applicant is aware of the need to amend inventorship; however, no such amendment is believed necessary based on this cancellation of claims.

Priority

Applicant acknowledges the Examiner's determination of the priority date of this application being the filing date of this application, April 6, 1999. To conform to this determination, Applicant has removed the paragraph claiming priority to other applications based on the amendment to the specification herein.

In that Applicant did not file a "bibliographic sheet" and in that the inclusion of an application data sheet is voluntary, it is believed that Applicant's amendment herein, which removes the paragraph claiming priority, is sufficient to comply with the Examiner's direction to correct the "relationship and status of other applications previously listed." (from page 3 of Final Office action, end of first paragraph under "Priority"). If other correction is required, Applicant respectfully requests that the Examiner so communicate this to Applicant.

Oath/Declaration

Applicant believes that Applicant has complied with the requirement to provide an executed Declaration by the inventors with the provision to the Patent Office on February 18, 2003 of the newly executed Declaration and Power of Attorney. However, the 05/05/2003 Final Office action contains a single sentence under this heading that ends in "... is required." It is believed this is a typographical error.

If other documentation is required as to the Oath/Declaration, Applicant respectfully requests that the Examiner so communicate this to Applicant.

Claim Rejections - 35 USC 103

The Examiner has maintained a rejection of claims 1-4, 8, 9, and 13-15 under 35 USC 103(c) as being obvious and therefore unpatentable in view of Yang *et al.*, Mack *et al.*, Kass-Eiler *et al.*, and Graham *et al.* (citations omitted, see page 5 of Final Office action).

By the amendments of claims herein, Applicant has confined the claims to include limitations that the packaging signals of the helper vectors are each flanked by at least one site specific recombinase target site (i.e., lox), such that action upon these by a recombinase enzyme (i.e., Cre recombinase) reduces the ability of that helper vector to be packaged. This, as described in the specification, helps lower the level of helper viral genome contamination (see specification, page 9, line 27, to page 10, line 2). In addition to these amendments, Applicant provides the following grounds and reasoning to prove that the above-noted Graham *et al.* reference is not properly combined with Yang *et al.*, Mack *et al.*, and Kass-Eiler *et al.* Accordingly, based on the amendments and arguments herein, the Applicant respectfully requests reconsideration of this rejection, and allowance of the claims now pending in this application.

First, it is recognized that the Examiner has rejected Applicant's previous assertion of a priority claim to application serial number 08/719,217. The above-noted Graham *et al.* patent application publication corresponds to application serial number 08/719,217. Because application serial number 08/719,217, in the Examiner's evaluation, did not contain sufficient disclosure of serial administration to allow it to be an application to which priority can be claimed, it follows that the corresponding Graham *et al.* patent application publication, WO 98/13510, does not contain a sufficient suggestion or motivation to combine the packaging-signal-flanked-by-recombinase-sites technology with the Yang *et al.*, Mack *et al.*, and Kass-Eiler *et al.* references. Therefore, it is inappropriate to use the Graham *et al.* patent application publication, WO 98/13510, in combination with any prior art reference in the above-noted 35 USC 103(c) obviousness rejection.

Second, it is noted that the lead inventor, Dr. Frank Graham, has communicated that is not aware of anyone practicing the invention prior to October 26, 1999. This date is the publication date of the first scientific article that used the invention of the present application. That first scientific article is:

Morral, N., O'Neal, W., Rice, K., Leland, M., Kaplan, J., Piedra, P. A., Zhou, H., Parks, R. J., Velji, R., Aguilar-Cordova, E., Wadsworth, S., Graham, F. L., Kochanek, S., Carey, K. D. and Beaudet, A. L. Administration of helper-dependent adenoviral vectors and

sequential delivery of different vector serotype for long-term liver-directed gene transfer in baboons. Proc. Natl. Acad. Sci. US 96: 12816-12821, 1999.

This further supports the arguments that:

- 1) Not considering the WO 98/13510 publication, it would not have been obvious to one of ordinary skill in the art to combine limitations in the prior art to achieve the present invention; and
- 2) Even considering the WO 98/13510 publication, because no one was observed to have practiced the invention in the time between the WO 98/13510 publication and October 26, 1999, it would not have been obvious to one of ordinary skill in the art to combine limitations in the prior art (including WO 98/13510) to achieve the present invention.

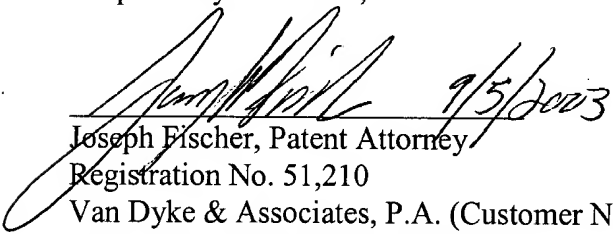
Thus, based on the amendments and one or both of the arguments above, reconsideration of the 35 USC 103(c) obviousness rejection is respectfully requested.

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All claims having either been placed in condition for allowance or cancelled, expedited passage of this case to issuance is respectfully solicited.

Applicant requests that the Examiner call the undersigned, at 888-416-1464, if clarification is needed on any aspect of this response, or if the Examiner believes that any valid basis of non-patentability remains after entrance and consideration of the remarks and amendments presented herein.

Respectfully submitted,

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